reporters attached to the solid substrates (beads). This ability enables the rapid determination of the presence or absence of a binding event and the identity of each bead (i.e., its reporter signature) after a bead has passed through the field of view (FOV). Hydrodynamic focussing ensures that the beads are at or near the focal plane of the imaging system. When required, an optical correction can be applied to account for minor changes in the location of the hydrodynamically focussed bead column. In addition, the imaging system can be constructed to view the beads from multiple angles to produce image data of a different fraction of the bead surface, to enable the construction of a three-dimensional representation of each bead. This configuration also enables correction of focus errors. The present invention spectrally decomposes the signal from each reporter in the axis perpendicular to flow and then forms an image of the reporters on a bead onto a single detector or multiple detectors. FIGURE 1 schematically illustrates this process.

As shown in FIGURE 1, a plurality of marked beads 11 pass through a sampling column 15 in a single file orientation. The imaging system shown includes a plurality of detectors 13, focussing elements or lenses 17, and one or more light source(s) 19. The location of the image on the detector is then determined by the spectral content of the signal emitted from the reporter as well as the spatial position of the reporter with respect to the bead. There are five embodiments of the present invention that accomplish the spectral decomposition and imaging of the beads.

First Embodiment for Spectral Decomposition and Imaging

A first embodiment of the system for spectral decomposition and imaging is shown in FIGURE 2A, and this embodiment is also disclosed in commonly assigned U.S. Patent No. 6,211,955, entitled "Imaging and Analyzing Parameters of Small Moving Objects Such as Cells," filed on March 29, 2000, the drawings and disclosure of which are hereby specifically incorporated herein by reference. In this previously filed application, there is no discussion of identifying reporters on beads. However, the following discussion describes how the apparatus disclosed in this previously filed application can be employed for spectral decomposition and imaging of objects such as beads and reporters included thereon. In regard to the present invention, a bead provided with reporters is simply a specific type of object. (It should be noted that where there is any variance between the description in any document incorporated herein by reference and the present disclosure, the present disclosure takes precedence.)

Although several types of pixelated detectors may be used in the present invention, in many cases a time delay integration (TDI) detector is preferable. The TDI detector preferably comprises a rectangular charge-coupled device (CCD) that employs a specialized pixel readout algorithm, as explained below. Non-TDI CCD arrays are

commonly used for two-dimensional imaging in cameras. In a standard CCD array, photons that are incident on a pixel produce charges that are trapped in the pixel. The photon charges from each pixel are readout of the detector array by shifting the charges from one pixel to the next, and then onto an output capacitor, producing a voltage proportional to the charge. Between pixel readings, the capacitor is discharged and the process is repeated for every pixel on the chip. During the readout, the array must be shielded from any light exposure to prevent charge generation in the pixels that have not yet been read.

In one type of TDI detector 44, which comprises a CCD array, the CCD array remains exposed to the light as the pixels are readout. The readout occurs one row at a time from the top toward the bottom of the array. Once a first row is readout, the remaining rows are shifted by one pixel in the direction of the row that has just been read. If the object being imaged onto the array moves in synchrony with the motion of the pixels, light from the object is integrated for the duration of the TDI detector's total readout period without image blurring. The signal strength produced by a TDI detector will increase linearly with the integration period, which is proportional to the number of TDI rows, but the noise will increase only as the square root of the integration period, resulting in an overall increase in the signal-to-noise ratio by the square root of the number of rows. One TDI detector suitable for use in the present invention is a Dalsa Corp., Type IL-E2 image sensor, although other equivalent or better image sensors can alternatively be used. The Dalsa image sensor has 96 stages or rows, each comprising 512 pixels; other types of image sensors useable in the present invention may have different configurations of rows and columns or a non-rectilinear arrangement of pixels. The Dalsa sensor has approximately 96 times the sensitivity and nearly 10 times the signal-to-noise ratio of a standard CCD array. The extended integration time associated with TDI detection also serves to average out temporal and spatial illumination variations, increasing measurement consistency.

It should be emphasized that the present invention is not limited to TDI detectors or CCD types of TDI detectors. Other types of TDI detectors, such as complementary metal oxide semiconductor (CMOS) and multi-channel plate imaging devices might also be used for the TDI detector in the present invention. It is important to understand that any pixelated device (i.e., having a multitude of light sensitive regions) in which a signal produced in response to radiation directed at the device can be caused to move through the device in a controlled fashion is suitable for use as the TDI detector in the present invention. Typically, the signal will move in synchrony with a moving image projected onto the device, thereby increasing the integration time for the image, without causing blurring. However, the motion of the signal can be

selectively desynchronized from the motion of the radiation image, as required to achieve a desired affect.

In imaging systems 45, 70, 250 in FIGURES 2C, 4, and 11 respectively, and in other embodiments of the present invention that employ a fluid flow to carry objects through the imaging system, a flow-through cuvette or a jet (not shown) contains the reporter labeled beads or other objects being analyzed. The velocity and cellular concentration of the fluid may be controlled using syringe pumps, gas pressure, or other pumping methods (not shown) to drive a sample solution through the system to match the pixel readout rate of the TDI detector. However, it should be understood that the readout rate of the TDI detector can be selectively controlled, as required, to match the motion of the sample solution.

As will be evident in FIGURE 2B, if the Figure depicts the imaging of object 24 over time, the object is shown at both a position 26 and a position 28 as it moves with fluid flow 22. As a consequence, images of object 24 will be produced on the detector at two discrete spatial positions 26′ and 28′, as indicated on the right side of FIGURE 2B. In the case of TDI detection, the signal on the detector can be made to move in synchronicity with image of object 24 such that signal is collected and integrated over the entire traversal of the detector. Alternatively, if FIGURE 2B is depicting a single instant in time, positions 26 and 28 can represent the location of two separate objects, which are simultaneously imaged on the detector at positions 26′ and 28′.

As shown in the FIGURE 2A, light from a column 22 of beads 24 that is hydrodynamically focussed to a well defined region, is collimated by passing through a collection lens 32. The light from the beads travels along a collection path 30. A spectral dispersing element 36 disposed in the collection path spectrally disperses the collimated light that has passed through the collection lens in a plane substantially orthogonal to a direction of relative movement between the beads and the imaging system, producing spectrally dispersed light. An imaging lens 40 is disposed to receive the spectrally dispersed light, producing an image from the spectrally dispersed light 38. Also included is a pixelated detector 44, disposed to receive the image produced by the imaging lens. As the movement occurs, the image of the bead produced by the imaging lens moves from row to row across the detector. As will be described earlier, the detector may be a TDI-type detector or a frame type detector, depending upon the specific embodiment.

As a result of light collimation by the collection lens in this embodiment, all light emitted from a first point in the bead travels in parallel rays. Light emitted from a second point in the bead will also travel in parallel rays, but at a different angle relative